THERAPEUTIC DRUG MONITORING AND SAFETY OF HIGH-DOSE AMIKACIN IN CRITICALLY ILL PATIENTS

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BACKGROUND

Pharmacokinetic parameters are altered in critically ill patient, such as increase of volume of distribution of hydrophillic drugs. Peak plasma levels of amikacin, a concentration dependent antibiotic, could be reduced in critically ill patients. Therefore, current recommendations include higher doses of amikacin (above 20 mg/kg/day) in critically ill patients in order to achieve therapeutic plasma levels, what means a possible higher incidence of adverse events, such as nephrotoxicity and ototoxicity. Therapeutic drug monitoring (TDM) and pharmacist intervention can be necessary in this type of patient to prevent these adverse effects.

PURPOSE

To assess the impact of TDM in critically ill patient receiving high dose amikacin.

MATERIAL AND METHODS

Retrospective descriptive study performed in a 400-bed tertiary hospital

- Inclusion criteria: critical patients receiving above 20mg/kg/day amikacin between January 2014-August 2017.
- Exclusion criteria: patients with a glomerular filtration rate(GFR) below 40 ml/min or receiving renal replacement therapy.
- An intermediate level (10-hour post-administration) was used to extrapolate almost all peak and trough levels. Peak levels above 50 mcg/ml and trough levels above 1 mcg/ml were considered supratherapeutic.
- Data collected: demographic, body max index(BMI), SOFA score (first 24h of amikacin therapy), sepsis, dosage, data extraction levels, renal function (serum creatinine(SCr) and GFR the first 24h of amikacin therapy and worst values during amikacin therapy), TDM recommendation.

Categorical variables presented as percentages, continuous variables as median and Q1-Q3 values.

RESULTS

Table 1. Demographic and clinical data

N	28
Sex (males)	18 (64.3)
Age (years)	76.5 (72-80)
Weight (kg)	75 (63.3-85.5)
BMI (Kg/m^2)	27.4 (24.8-32.1)
Adjusted weight (kg)	69.2 (60.8-75.1)
SOFA score	4 (3-6)
Sepsis (n)	20 (71.4)
Septic shock (n)	3 (10.7)
Dosage (mg/kg/24h)	21.5 (20-25)
Supratherapeutic peak (> 50 mcg/ml) (n)	21 (75)
Supratherapeutic trough (> 1mcg/ml) (n)	22 (78.6)

Table 2. Renal function data

SCr (initial) (mg/dL)	0.76 (0.65-0.85)
SCr (worst)(mg/dL)	1.1 (0.87-1.23)
GFR (initial) (ml/min)	88 (77.9-90.1)
GFR (worst) (ml/min)	59 (46-72.8)
Day worst GFR/SCr value (n)	2 (1-4.3)

Figure 1. RIFLE-score after amikacin therapy

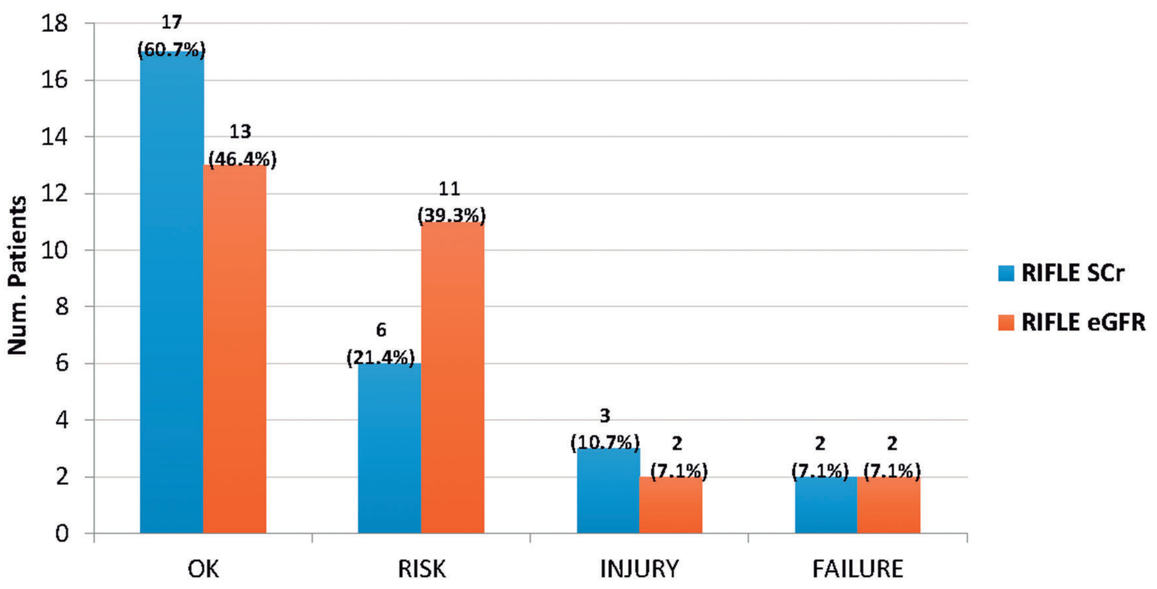


Figure 2. Interval recommendation

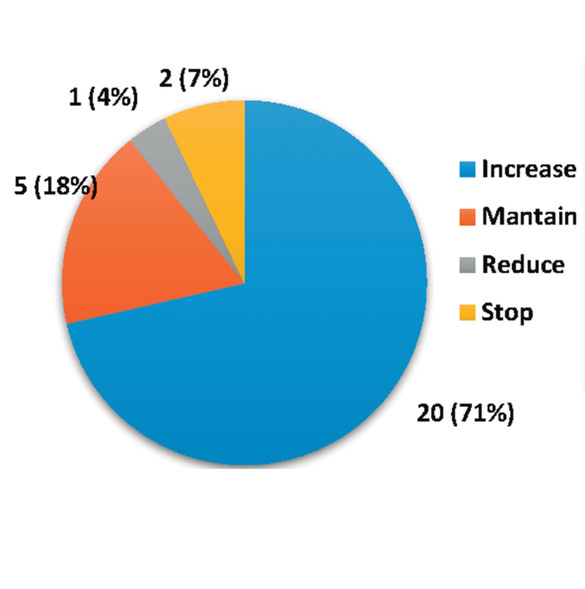
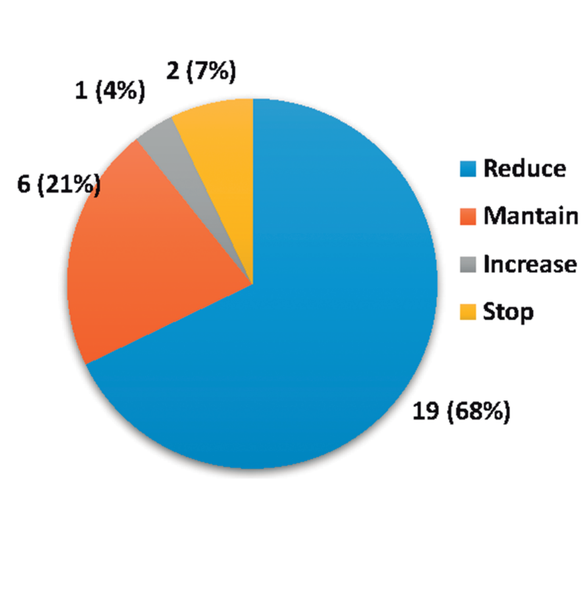


Figure 3. Dosage recommendation



CONCLUSIONS

- Greater part of patients with current recommendation of high doses of amikacin presented supratherapeutic plasma levels of amikacin and about 70% of patients needed a dose reduction or an interval increase.
- Therapeutic drug monitoring after first dose should be a regular practice in critically ill patient, which present an early decline in renal function during amikacin therapy.